CLAIMS

1. The use of a γδ T cell activator, together with a pharmaceutically acceptable carrier, for the manufacture of a pharmaceutical composition for the treatment of a solid tumor in a warm-blooded animal in need of such treatment.

2. A method for treating a solid tumor, said method comprising the step of administering to a warm-blooded animal, in at least one treatment, a therapeutically effective amount of a γδ T cell activator, together with a pharmaceutically acceptable carrier, to a warm-blooded animal in need of such treatment.

3. The use of claim 1, wherein at least two treatments are administered to said animal.

4. The use of claim 1, wherein at least three treatments are administered to said animal.

5. The use of claim 1, wherein at least four treatments are administered to said animal.

6. The use of claim 1, wherein at least six treatments are administered to said animal.

7. The use of any one of the above claims, wherein the γδ T cell activator is administered in more than one treatment with an interval of about two to about eight weeks between treatments.

8. The use of any one of the above claims wherein the γδ T cell activator is administered in more than one treatment with an interval of about three to about four weeks between treatments.

9. The use of a γδ T cell activator, together with a pharmaceutically acceptable carrier, for the manufacture of a pharmaceutical composition for the treatment of a tumor in a warm-blooded animal in need of such treatment, wherein the γδ T cell activator is administered in more than one treatment with an interval of about two weeks to about eight weeks between treatments.

10. The use of claim 9, wherein at least two treatments are administered to said animal.

11. The use of claim 9, wherein at least three treatments, preferably at least four treatments, are administered to said animal.

12. The use of claims 9, wherein at least six treatments are administered to said animal.

13. The use of claims 9 to 12, wherein the tumor is a haematological tumor.

14. The use of claims 9 to 12, wherein the tumor to be treated is a lymphoma.

15. The use of claims 9 to 12, wherein the tumor is a solid tumor.

16. The use of any one of the above claims, wherein the biological activity of γδ T cells are increased in said warm-blooded animal or said subject.

17. The use of any one of the above claims, wherein the number of circulating γδ T cells are increased in said warm-blooded animal or said subject.

18. The use of any one of the above claims, wherein said γδ T cell activator is administered in an amount sufficient to expand the γδ T cell population in a subject to reach between 30-90% of total circulating lymphocytes

19. The use of any one of the above claims, wherein said γδ T cell activator is administered in an amount sufficient to induce an at least 10-fold increase in the γδ T cell population in a subject.

20. The use of any one of the above claims, wherein the tumor is a metastatic tumor, wherein the γδ T activator is administered to a human in need of such treatment in a dose that is appropriate for the treatment of said disease.

21. The use of claims 1 to 8, 15 to 20, wherein the tumor to be treated is selected from the group consisting of lung, colorectal, prostate, breast or epidermoid head or neck tumors.

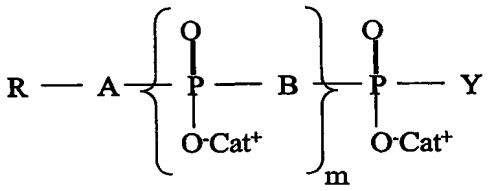
22. The use of claims 1 to 8, 15 to 20 where the tumor to be treated is a renal cancer.

23. The use of claims 1 to 8, 15 to 20 where the tumor to be treated is a metastatic renal cancer.

24. The use of claims 1 to 8, 15 to 20 where the proliferative disease to be treated is selected from the group consisting of a melanoma, ovarian cancer, pancreas cancer, neuroblastoma, head or neck cancer, bladder cancer, renal cancer, brain cancer and gastric cancer.

25. The use of any one of the above claims wherein the γδ T cell activator is a composition comprising a compound capable of inducing the proliferation of a γδ T cell in a pure population of γδ T cell clones when said compound is present in culture at a concentration of less than 1 mM.

26. The use of any one of the above claims wherein the γδ T cell activator is a composition comprising a compound of formula (I) :



Formula (I)

wherein Cat+ represents one (or several, identical or different) organic or mineral cation(s) (including proton);

m is an integer from 1 to 3;

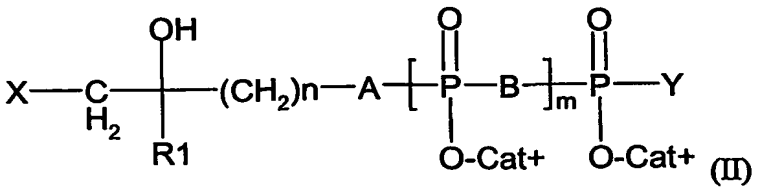
B is O, NH, or any group capable to be hydrolyzed;

Y = O^-Cat^+, a C_1-C_3 alkyl group, a group -A-R, or a radical selected from the group consisting of a nucleoside, an oligonucleotide, a nucleic acid, an amino acid, a peptide, a protein, a monosaccharide, an oligosaccharide, a polysaccharide, a fatty acid, a simple lipid, a complex lipid, a folic acid, a tetrahydrofolic acid, a phosphoric acid, an inositol, a vitamin, a co-enzyme, a flavonoid, an aldehyde, an epoxyde and a halohydrin;

A is O, NH, CHF, CF_2 or CH_2; and,

R is a linear, branched, or cyclic, aromatic or not, saturated or unsaturated, C_1-C_{50} hydrocarbon group, optionally interrupted by at least one heteroatom, wherein said hydrocarbon group comprises an alkyl, an alkylenyl, or an alkynyl, preferably an alkyl or an alkylene, which can be substituted by one or several substituents selected from the group consisting of : an alkyl, an alkylenyl, an alkynyl, an epoxyalkyl, an aryl, an heterocycle, an alkoxy, an acyl, an alcohol, a carboxylic group (-COOH), an ester, an amine, an amino group ($-NH_2$), an amide ($-CONH_2$), an imine, a nitrile, an hydroxyl (-OH), a aldehyde group (-CHO), an halogen, an halogenoalkyl, a thiol (-SH), a thioalkyl, a sulfone, a sulfoxide, and a combination thereof.

27. The use of claim 26, where the γδ T cell activator is a composition comprising a compound of formula (II):



(II)

in which X is an halogen (preferably selected from I, Br and Cl), B is O or NH, m is an integer from 1 to 3, R1 is a methyl or ethyl group, Cat+ represents one (or several, identical or different) organic or mineral cation(s) (including the proton), and n is an integer from 2 to 20, A is O, NH, CHF, CF_2 or CH_2, and Y is O^-Cat+, a nucleoside, or a radical –A-R, wherein R is selected from the group of 1), 2) or 3).

28. The use of claim 27, wherein the compound of formula (II) is BrHPP.

29. The use of claim 27, wherein the compound of formula (II) is CBrHPP.

30. The use of claim 27, wherein the compound of formula (II) is epoxPP.

31. The use of claims 27 to 30 wherein the γδ T cell activator is administered in a dose to humans between 10 mg/kg to 100 mg/kg.

32. The use of claims 27 to 30 wherein the γδ T cell activator is administered in a dose to humans that is calculated according to the formula (I) single dose (mg/kg)=(10 to y) * N (I) where N is the number of weeks between treatments and y is 100.

33. The use of claim 32 wherein the γδ T cell activator is administered in a dose to humans that is calculated according to the formula (I): single dose (mg/kg)=(5 to 60) * N (I).

34. The use of claims 27 to 30, wherein said γδT activator is administered by intravenous infusion in a dose to humans that is calculated according to the formula (I): single dose (mg/kg)=(10 to 100) * N (I), where N is the number of weeks between treatments such that N is between about 3 and about 4.

35. The use of a CBrHPP compound for the manufacture of a pharmaceutical composition for regulating Vγ9/Vδ2$^+$ T cells in a human subject, wherein the CBrHPP compound is administered into said subject at a dose of between 10 mg/kg to 100 mg/kg of said compound per kilogram of the subject's weight.

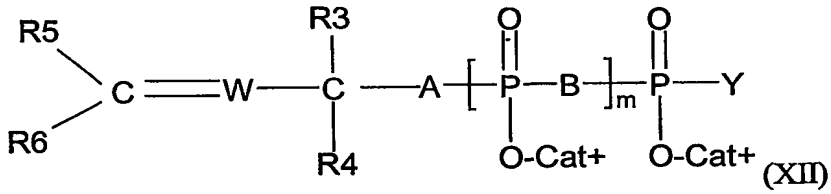
36. The use of a CBrHPP compound for the manufacture of a pharmaceutical composition for regulating $V\gamma9/V\delta2^+$ T cells in a human subject, wherein the CBrHPP compound is administered into said subject at a dose of between 10 mg/kg to 100 mg/kg of said compound per kilogram of the subject's weight within a period of less than 24 hours.

37. The use of claims 27 to 36 wherein the γδ T cell activator is administered in a dose to humans between 5 mg/kg to 60 mg/kg.

38. The use of claims 27 to 36 wherein the γδ T cell activator is administered in a dose of about 20 mg/kg.

39. The use of a compound according to claim 27, for the manufacture of a pharmaceutical composition for stimulating a γδ T cell in a warm-blooded animal, wherein said compound is administered to the warm-blooded animal in more than one treatment, with an interval of about two weeks to about eight weeks between treatments.

40. The use of claim 26, wherein the γδ T cell activator is a composition comprising a compound of formula (XII):



(XII)

in which R_3, R_4, and R_5 , identical or different, are a hydrogen or (C_1-C_3)alkyl group, W is –CH- or –N-, R_6 is an (C_2-C_3)acyl, an aldehyde, an (C_1-C_3)alcohol, or an (C_2-C_3)ester, Cat+ represents one (or several, identical or different) organic or mineral cation(s) (including the proton), B is O or NH, m is an integer from 1 to 3, A is O, NH, CHF, CF_2 or CH_2, and Y is O^-Cat+, a nucleoside, or a radical –A-R, wherein R is selected from the group of 1), 2) or 3).

41. The use of claim 40, wherein the compound of formula (XII) is HDMAPP.

42. The use of claim 40, wherein the compound of formula (XII) is CHDMAPP.

43. The use of claims 40 to 42 wherein the γδ T cell activator is administered in a dose to humans that is calculated according to the formula (I): single dose (mg/kg)=(0.001 to y) * N (I), where N is the number of weeks between treatments and y is 100.

44. The use of claim 43 wherein the γδ T cell activator is administered in a dose to humans that is calculated according to the formula (I): single dose (mg/kg)=(0.01 to 20) * N (I).

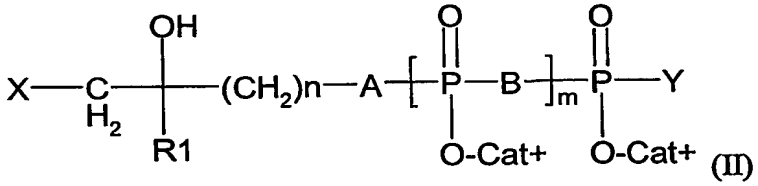
45. The use of claim 43 wherein the γδ T cell activator is administered in a dose to humans that is calculated according to the formula (I) single dose: (mg/kg)=(0.01 to 5) * N (I).

46. The use of claim 43 wherein the γδ T cell activator is administered in a dose to humans that is calculated according to the formula (I) single dose: (mg/kg)=(0.02 to 5) * N (I).

47. The use of claims 40 to 42 wherein the γδ T cell activator is administered in a dose to humans between 10 μg/kg to 20 mg/kg.

48. The use of claims 40 to 42 where said γδT activator is administered by intravenous infusion in a dose to humans that is calculated according to the formula (I) single dose (mg/kg)=(0.01 to 20) * N (I) where N is the number of weeks between treatments such that N is between about 3 and about 4.

49. The use of a compound of formula (II):



(II)

in which X is an halogen (preferably selected from I, Br and Cl), B is O or NH, m is an integer from 1 to 3, R1 is a methyl or ethyl group, Cat+ represents one (or several, identical or different) organic or mineral cation(s) (including the proton), and n is an integer from 2 to 20, A is O, NH, CHF, CF_2 or CH_2, and Y is O^-Cat+, a nucleoside, or a radical –A-R, wherein R is selected from the group of 1), 2) or 3),

for the manufacture of a pharmaceutical composition for regulating $V\gamma9/V\delta2^+$ T cells in a human subject, wherein said compound is administered into said subject at a dose of between 10 μg/kg to 20 mg/kg of said compound per kilogram of the subject's weight.

50. The use of a HDMAPP or CHDMAPP compound for the manufacture of a pharmaceutical composition for regulating $V\gamma9/V\delta2^+$ T cells in a human subject, wherein the HDMAPP or CHDMAPP compound is administered into said subject at a dose of between 10 μg/kg to 20 mg/kg of said compound per kilogram of the subject's weight.

51. The use of a HDMAPP or CHDMAPP compound for the manufacture of a pharmaceutical composition for regulating Vγ9/Vδ2$^+$ T cells in a human subject, wherein the HDMAPP or CHDMAPP compound is administered into said subject at a dose of between 10 μg/kg to 20 mg/kg of said compound per kilogram of the subject's weight within a period of less than 24 hours.

52. The use of claims 50 or 51 wherein the γδ T cell activator is administered in a dose to humans between 10 μg/kg to 5 mg/kg.

53. The use of claims 50 or 51 wherein the γδ T cell activator is administered in a dose to humans between 10 μg/kg to 2.5 mg/kg.

54. The use of claims 50 or 51 wherein the γδ T cell activator is administered in a dose to humans between 10 μg/kg to 1 mg/kg.

55. The use of any one of the above claims, further comprising separately administering to a subject in need thereof an effective amount of a γδT activator and an interleukin-2 polypeptide.

56. The use of claim 55, wherein the interleukin-2 polypeptide is administered over a period of time comprised between 1 and 10 days.

57. The use of a γδ T cell activator and an interleukin-2 polypeptide, for the manufacture of a pharmaceutical composition for regulating the activity of γδ T cells in a mammalian subject, the γδ T cell activator and interleukin-2 polypeptide being administered separately to the subject and the interleukin-2 polypeptide is administered over a period of time comprised between 1 and 10 days.

58. A method for stimulating a γδ T cell in a subject, comprising separately administering to a subject in need thereof an effective amount of a γδT activator and an interleukin-2 polypeptide, wherein the interleukin-2 polypeptide is administered over a period of time comprised between 1 and 10 days.

59. A method of treating a cancer, an infectious disease, an autoimmune disease or an allergic disease in a subject, comprising separately administering to a subject in need thereof an effective amount of a γδT activator and an interleukin-2 polypeptide, wherein the interleukin-2 polypeptide is administered over a period of time comprised between 1 and 10 days.

60. The use of any one of the above claims, wherein the interleukin-2 polypeptide is administered at low doses.

61. The use of any one of the above claims, wherein the interleukin-2 polypeptide is administered at a daily dose comprised between 0.2 and 2 MU per day, even more preferably between 0.2 and 1.5 MU, further preferably between 0.2 and 1 MU.

62. The use of any one of the above claims, wherein the daily dose of interleukin-2 polypeptide is administered as a single injection or in two injections.

63. The use of any one of the above claims, wherein the γδ T cell activator is administered as a single dose at the beginning of the treatment.

64. The use of any one of the above claims, wherein the γδ T cell activator is administered as a single dose at the beginning of the treatment and the interleukin-2 polypeptide is administered on at least 2 days during within 10 days from said beginning of the treatment.

65. The use of any one of the above claims, wherein the γδ T cell activator is a ligand of the T receptor of γδ T lymphocytes.

66. The use of any one of the above claims, wherein the γδ T cell activator is a PED or PHD compound and is administered as a single injection at a dose comprised between 10 and 50 mg/kg, at the beginning of the treatment, and wherein the interleukin-2 polypeptide is administered at a daily dose comprised between 0.2 and 2 MU per day over a period of time comprised between 1 and 10 days.

67. The use of any one of the preceding claims, wherein the subject is a human subject having a cancer, an infectious disease, an auto-immune disease or an allergic disease.

68. The use of a γδ T cell activator and an interleukin-2 polypeptide, for the manufacture of a pharmaceutical composition for treating cancer in a subject, wherein said synthetic γδ T activator and interleukin-2 polypeptide are administered separately to the subject.

69. The use of a γδ T cell activator and an interleukin-2 polypeptide, for the manufacture of a pharmaceutical composition for treating an infectious disease in a subject, wherein said synthetic γδ T activator and interleukin-2 polypeptide are administered separately to the subject.

70. The use of a γδ T cell activator and an interleukin-2 polypeptide, for the manufacture of a pharmaceutical composition for treating an autoimmune disease in a subject, wherein said synthetic γδ T activator and interleukin-2 polypeptide are administered separately to the subject.

71. The use of a γδ T cell activator and an interleukin-2 polypeptide, for the manufacture of a pharmaceutical composition for treating a disease caused by or associated with pathological cells sensitive to lysis by γδ T cells in a subject, wherein said synthetic γδ T activator and interleukin-2 polypeptide are administered separately to the subject.

72. A product comprising a γδ T cell activator and an interleukin-2 polypeptide, for separate use, for regulating the activity of γδ T cells in a mammalian subject.

73. The use of an γδ T activator for the manufacture of a pharmaceutical preparation for the treatment of a solid tumor, comprising admixing said γδ T activator with a pharmaceutically acceptable carrier.

74. The use of a γδ T cell activator and an interleukin-2 polypeptide, for the manufacture of a pharmaceutical composition for regulating the activity of γδ T cells in a mammalian subject, the γδ T cell activator and interleukin-2 polypeptide being administered separately to the subject.

75. The use of any one of the above claims where the γδ T cell activator is administered by intravenous infusion.

76. The use of any one of the above claims wherein each infusion takes place during about 5 to about 120 min.

77. The use of any one of the above claims wherein each infusion takes place during about 5 to about 30 min..

78. A pharmaceutical composition containing a therapeutically effective amount of CHDMAPP as an active ingredient, together with a pharmaceutically acceptable carrier.

79. A pharmaceutical composition containing a therapeutically effective amount of CBrHPP as an active ingredient, together with a pharmaceutically acceptable carrier.